PHYSIOLOGY OF THE RESPIRATORY SYSTEM

No. 436R2

Activated: 7/1/64
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THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

SUCCESSOR TO THE
TOBACCO INDUSTRY RESEARCH COMMITTEE
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COMMITTEE:
Dr. Bing, Chm.
Dr. Cattell
Dr. Jacobson

Application for Renewal of Research Grant

Date: January 17, 1966

1. Name of Investigator: Domingo M. Aviado, M.D.

2. Title: Professor of Pharmacology

3. Institution & Address: University of Pennsylvania School of Medicine
Department of Pharmacology
36th & Hamilton Walk
Philadelphia, Pennsylvania 19104

4. Project or Subject: Effects of nicotine and cigarette smoking on neurogenic mechanisms in the lung.

5. Detailed Plan of Procedure (Use additional pages if more space is required.)

Our progress report which is being submitted with this proposal consists of four published articles on the bronchopulmonary[1-4] effects of tobacco, and of three manuscripts (submitted for publication) on the cardiopulmonary[5-7] effects of tobacco. These articles deal on work during the past two years and have served the purpose of establishing the existence of neurogenic and humoral mechanisms in the lung which are activated by cigarette smoking and elicit changes in bronchomotor tone, bronchial blood flow, pulmonary blood pressure, cardiac output, and coronary vascular resistance. The major theme of the experiments proposed for the third year is on the effects of tobacco on respiratory control, blood-gas exchange and pulmonary compliance and resistance to breathing. The details of the poposed experiments are as follows:

a. Respiratory control. The participation of the medullary centers and chemoreceptors to the respiratory effects of tobacco will be investigated in the anesthetized dog. Since most of previous experiments are on nicotine, the planned experiments will be on the effects of blood exposed to cigarette smoke directly on the respiratory center and on the chemoreceptors in the carotid, aortic and pulmonary bodies. The perfusion and cross circulation technics will be applied to these areas to assess the relative importance of centra and receptor mechanisms.

b. Blood gas exchange. The tension of oxygen and carbon dioxide of blood from the lung exposed to cigarette smoke will be measured. The apparatus for direct polarographic methods has been assembled and ready to apply to blood samples collected from the anesthetized dog. Special attention will be paid to the participation of arteriovenous communications and bronchopulmonary blood vessels in contributing to the venous admixture in the pulmonary veins.

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c. Pulmonary compliance and resistance. Dogs and smaller animals will be exposed daily to cigarette smoke. Pulmonary compliance and airway resistance will be measured daily. After the appearance of significant alterations in lung function, the animal will be anesthetized and measurements taken with the open chest. Finally the lung will be excised and artifically perfused for comparison with the lung excised from the animal not previously exposed to cigarette smoke. The tissue will also be examined histologically for lesions in the pulmonary blood vessels and bronchibles.

The senior investigator is hopeful that after the information from the proposed experiments become available, plans for a second three-year project devoted to the relationship of tobacco to the pathogenesis of chronic pulmonary emphysema, bronchial spasm and bronchial neoplasm can be formulated.

References cited above and submitted as progress report no. 2.

1. Aviado, D. M. and Samanek, M.: Bronchopulmonary Effects of Tobacco and Related Substances: I. Bronchoconstriction and Bronchodilatation: Influence of Lung Denervation. Arch Environ Health 11: 141-151, 1965.

2. Samanek, M., and Aviado, D. M.: Bronchopulmonary Effects of Tobacco and Related Substances: II. Bronchial Arterial Injections of Nicotine and Histamine. Arch Environ Health 11: 152-160, 1965

3. Samanek, M., Aviado, D. M. and Peskin, G. W.: Bronchopulmonary Effects of Tobacco and Related Substances: III. Axon Reflexes Elicited from the Visceral Pleura. Arch Environ Health 11: 160-166, 1965.

4. Samanek, M. and Aviado, D. M.: Bronchopulmonary Effects of Tobacco and Related Substances: IV. Bronchial Vascular and Bronchomotor Responses; Their Suggested Defense Function. Arch Environ Health 11: 167-176, 1965.

5. Aviado, D. M., Samanek, M. and Folle, L. E.: Cardiopulmonary Effects of Tobacco and Related Substances: I. The Release of Histamine During Inhalation of Cigarette Smoke and Anoxemia in the Heart-Lung Preparation. To be submitted to the Arch Environ Health.

6. Folle, L. E., Samanek, M. and Aviado, D. M.: Cardiopulmonary Effects of Tobacco and Related Substances: II. Coronary Vascular Effects of Cigarette Smoke and Nicotine. To be submitted to the Arch Environ Health.

7. Samanek, M. and Aviado, D. M.: Cardiopulmonary Effects of Tobacco and Related Substances: III. Pulmonary Vascular Effects of Cigarette Smoke and Nicotine. To be submitted to the Arch Environ Health.

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6. Budget Plan:

	Salaries	9,000
a.	Salaries (9% employee benefits)	810
b.	Expendable Supplies	4,600
c.	Other Expenses	2,000
d.	Permanent Equipment	500
e.	Overhead (15% of a, b, c)	2,340
	Total	19,250

7. Anticipated Duration of Work:

One year

8. Facilities and Staff Available: We have increased our original yearly budget by 50% chiefly because we would like to embark on this project more extensively than we have for the past two years. The requested amount for salaries will be for a postdoctorate fellow ($5,000) and a technician ($4,000) who will spend full time on this project, under the supervision of the Director of the project. The expendable supplies will largely be for the cost of animals (dogs, rabbits, rats and guinea pigs). The additional pieces of permanent equipment will include microtone and microscope for examining lung tissue section.

9. Additional Requirements:

None

10. Additional Information (Including relation of work to other projects and other sources of support):

This request is not being covered by other sources of support. The undersigned has a grant of $49,000 annually from the Department of the Army for the project entitled "Pharmacology of New Antimalarials."

Signature Gino M. Cerio, M.D.
Director of Project

Luther L. Terry, M.D.
Vice President for Medical Affairs

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